REMARKS

Receipt of the Office Action mailed October 2, 2003 is acknowledged. The figures and specification have been amended to address various issues raised in the Office Action. Claims 1-6, 9 and 10 have been amended. Claims 1 and 2 have been amended to further clarify what applicant regards as the invention and does not narrow the scope of the claims because the amendments make explicit that which was implicit. Claims 3, 4 and 5 have been amended to correct an obvious error and do not narrow the scope of the claims. Claim 9 has been amended in response to the 35 USC 101 rejection raised in the Office Action. Support for the amendments can be found throughout the specification. For example, support for the amendment to Claim 9 can be found at page 13, lines 10-14. No new matter is believed to be added. Upon entry of the amendment, claims 1-10 will be pending in the application.

On page 2 of the Office Action, Figures 2, 3 and 7 are objected to as not being separately labeled. Enclosed herewith are replacement sheets containing Figures 2A and B, 3A and B and 7A and B, correctly labeled. Also enclosed is a replacement sheet containing Figure 1 showing the vertical lines and arrows referred to on page 6, lines 16-19 of the specification. Applicants submit that this does not present new matter in that the normal CRP range for human sera is well known in the art. See, for example, the Tietz textbook of Clinical Chemistry, 2nd edition, pg. 714. With regard to the arrows, in corrected Figure 1, they simply reference on the x axis where the CRP5-10 and CRP5-23 lines intersect the 50% inhibition line.

Claims 3, 4, 6-8 and 10 stand rejected under 35 U.S.C. section 112, first paragraph as lacking adequate written description and lacking enablement. Reconsideration and withdrawal of the rejection are respectfully requested. Applicants submit that the hybridomas cited were deposited with the ATCC prior to the filing date of the application, in accordance with the Budapest Treaty Rules. Applicants enclose as Exhibit A a copy of the Certificate of Deposit from

the ATCC, and the specification has been amended to provide the additional information required by the Rules.

In addition, Applicants make the assurance under 37 CFR 1.808 that: access to the deposit will be available during the pendency of the present application to one determined by the Commissioner to be entitled thereto under section 1.14 and 35 U.S.C. section 122; and subject to the restrictions set forth in 37 CFR 1.808(b), all restrictions imposed by applicant on the availability to the public of the deposited material will be irrevocably removed upon the granting of the patent on the present application. Therefore, Applicants respectfully request that the Examiner withdraw the rejection.

Claims 1-10 stand rejected under 35 U.S.C. section 112, second paragraph as failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. With regard to the rejection of claims 1-5, 9 and 10 based on the alleged lack of interrelationship of the components, Applicants have amended method claims 1 and 2 to further clarify the role of the antiidiotypic antibody and the anti-human C-reactive protein antibody and how they interact with each other and the C-reactive protein antigen. With regards to claims 5, 9 and 10, Applicants submit that further amending these claims to describe interrelationships is not required under section 112, second paragraph, since these claims are merely claiming components of the present invention. In view of the foregoing and the other clarifying amendments to the claims, Applicants submit that the rejections under Section 112, second paragraph have been obviated.

Claim 9 stands rejected under 35 U.S.C. section 101 as being directed to non-statutory subject matter. Applicants have amended claim 9 to recite that the antiidiotypic antibody is isolated and purified. In addition, claim 9 has also been amended to recite an antiidiotypic antibody raised against a low affinity anti-human C-reactive protein antibody, which is capable of binding to CRP5-23 with relatively

high affinity (Kd < 10^{-8}M), and its binding to CRP5-23 is mutually exclusive with binding of C-reactive protein. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

Claims 6-8 stand rejected under 35 U.S.C. section 102(b) or under 35 U.S.C. section 103(a) over either Kilpatrick et al. ("Kilpatrick") or Siegel et al. ("Siegel"). Reconsideration and withdrawal of the rejection are respectfully requested.

The Examiner asserts that Kilpatrick or Siegel anticipates the invention set out in claims 6-8, or alternatively, renders those claims obvious. With regard to anticipation, claims 6-8 recite a specific hybridoma cell line CRP5-23 (ATCC No. PTA-1354). These hybridomas generate the low affinity anti-human C-reactive protein antibody. There is nothing in the disclosure of Kilpatrick or Siegel that indicates that the HD2-4 antibody or hybridoma is the same as the claimed antibodies or cell line. Siegel at page 9 under "Detailed Description of Preferred Embodiments" describes production of hybridomas. Both the present invention and prior art are the same in that cells from animals immunized with CRP are fused with cells such as mylemoa cells. However, this is where all similarity ends. In the present invention, the resulting hybridomas were screened for antibodies having a low affinity for CRP, which is an important aspect of the present invention. In Siegel or Kilpatrick, there is no indication that the hybridomas will produce antibodies having these properties. Thus, there is no *prima facie* case of anticipation.

With regards to obviousness, as noted above, an important aspect of the present invention are antibodies having a low affinity for CRP. The problem to be solved by the present invention that the prior art applied by the Examiner or elsewhere fails to achieve, is to measure high concentrations of large molecules such as CRP. See, e.g., the present application at page 2, lines 5-14, which describes known assays as being applied to high concentration, low molecular

weight drugs. As the same paragraph indicates, a problem encountered in making suitable antibody and labels for analytes lies in providing the proper affinity requirements. Page 2, line 26 to page 3, line 15 teaches that this is particularly difficult to achieve with high concentration, high molecular weight analytes, such as CRP, because conventional immunoassays will require large amounts of labeled antibody.

The present invention solves the foregoing problem by providing a novel antibody (CRP5-23) which has a relatively low affinity for CRP, but a higher affinity to the novel labeled antibody (the antiiodiotypic antibody raised against CRP5-23). See, e.g., page 4, lines 11-19, which describes the low affinity CRP5-23 antibody. Also Figure 1, demonstrates that CRP5-23 has a low binding affinity at greater than 10^{-7} M CRP. This allows the measurement of high concentrations large molecular weight analytes using relatively low concentrations of labeled antibodies. See, e.g., page 18, lines 20-24.

An additional, unexpected advantage of the novel antibody is that it is insensitive to ionized calcium when binding to CRP. As explained at page 5, lines 6-21, the conformation of CRP is dependent on calcium. Thus, the insensitivity of the antibody to calcium assures that the binding of the antibody to CRP will not be compromised to varying levels of calcium that may be present.

Siegel or Kilpatrick fail to disclose a solution to, or even recognize the problem of measuring high concentration, high molecular weight analytes. Thus, there would have been no motivation to one skilled in the art to "modify" the hybridomas disclosed in Siegel or Kilpatrick to result in a hybridoma producing antibodies having a low affinity for CRP. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

Claims 1-5, 9 and 10 stand rejected under 35 U.S.C. section 103(a) as being unpatentable over Englebienne in view of Goldstein, Maggio, or Potocnjak

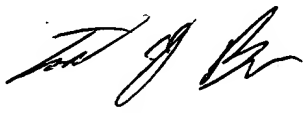
et al. ("Potocnjak") and further in view of Siegel. Reconsideration and withdrawal of the rejection are respectfully requested.

As noted above, the problem to be solved by the present invention that the prior art applied by the Examiner or elsewhere fails to achieve, is to measure high concentrations of large molecules such as CRP. The primary reference of Englebienne is applied by the Examiner as teaching measurement of CRP by competitive immunoassays. However, Englebienne measures through the use of highly labeled soluble polymers which is different than antibody-antiidiotypic antibody format presently claimed. The secondary references of Goldstein, Maggio or Potocnjak teach the use of antiiodiotypic antibodies in assays, however, they are limited to low concentrations of analytes. Thus, the combination of prior art applied by the Examiner fails to teach or suggest the novel antibody that has a low affinity that is able to measure high concentrations of high molecular weight analytes, such as CRP as claimed. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

The examination of these claims and passage to allowance are respectfully requested. An early Notice of Allowance is therefore earnestly solicited. Applicants invite the Examiner to contact the undersigned at (732) 524-1496 to clarify any unresolved issues raised by this response.

The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Account No. 10-0750/CDS 0236/TJB. This sheet is submitted in triplicate.

Respectfully submitted,



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